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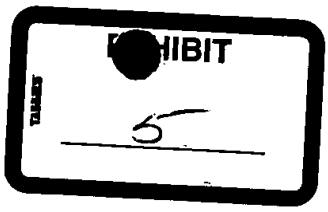


# Acute Platelet Inhibition With Abciximab Does Not Reduce In-Stent Restenosis (ERASER Study)

The ERASER Investigators*

*Background*—Although stents reduce restenosis compared with balloon angioplasty, their long-term efficacy is limited by neointimal hyperplasia. Platelet and $\alpha_v\beta_3$ integrin receptor inhibition limits neointimal proliferation in animal models of arterial injury.

*Methods and Results*—We tested whether the dual $\beta_3$ integrin blocking agent abciximab, administered for 12 or 24 hours at the same intravenous dose as that shown to reduce adverse clinical events (death, infarction, and revascularization) after angioplasty, would reduce restenotic tissue volume, as measured by intravascular ultrasound at 6 months. Two hundred twenty-five patients were randomly allocated to placebo or abciximab before coronary intervention. Of the 215 patients who received stents and study drug, 191 (88.8%) returned for late (≥4 months) coronary evaluation. Tissue volume, expressed as a percentage of stent volume, did not differ: 25±15%, 27±15%, and 29±14% for the patients in the placebo and the 12- and 24-hour abciximab groups, respectively. Lack of abciximab benefit was confirmed by quantitative coronary angiography (dichotomous restenosis: 11.6%, 18.9%, and 19.4%; loss index: 0.33, 0.52, and 0.47, respectively, $P$=NS).

*Conclusions*—Potent platelet inhibition with abciximab, as administered in this study, does not reduce in-stent restenosis. The interrelationship between stents, platelets, and neointimal proliferation requires further study. (*Circulation*. 1999;100:799-806.)

**Key Words:** angioplasty ■ stents ■ platelets ■ glycoproteins ■ vitronectin

Intracoronary stents reduce the absolute incidence of restenosis compared with balloon angioplasty in selected patients and lesions by 10% to 15% and improve 6-month event-free survival by 10% to 19%.[1,2] Stents reduce restenosis by an improvement in initial lesion cross-sectional area, but stenting aggravates the neointimal hyperplasia and the late lumen loss compared with that after angioplasty alone.[1]

Reduction of neointimal hyperplasia after stent placement should greatly retard clinical restenosis. Schwartz et al[3] and Miller et al[4] described the chronology of in-stent restenosis in animal models as early thrombosis, followed by thrombus endothelialization and infiltration by lymphocytes and monocytes, and finally smooth muscle cell migration into the resolving thrombus and proliferation. Ligand binding to $\alpha_{IIb}\beta_3$ (glycoprotein IIb/IIIa) and $\alpha_v\beta_3$ (vitronectin) receptors mediates platelet aggregation and smooth muscle cell migration, respectively, both of which appear to be involved in the restenosis process.[5] Combined inhibition of both integrins,[6] specific inhibition of $\alpha_v\beta_3$,[7–11] and profound antibody-induced thrombocytopenia[12] inhibit neointimal thickening after arterial injury in animal models. Abciximab inhibits both integrins and has been shown to decrease the incidence of target lesion revascularization (TLR) after angioplasty.[13] Abciximab also cross-reacts with the leukocyte integrins Mac-1 and intracellular adhesion molecule-1, which mediate inflammation after arterial injury and may be involved in restenosis.[14,15]

We hypothesized that intravenous abciximab might diminish neointimal hyperplasia after intracoronary stenting in humans. This study was designed to test that hypothesis, determining neointimal hyperplasia by measuring in-stent volume obstruction by 3D arterial reconstruction of intravascular ultrasound (IVUS) images.

## Methods

### Study Design and Study Population

The Evaluation of ReoPro® And Stenting to Eliminate Restenosis (ERASER) study was a double-blind, placebo-controlled randomized trial carried out at 17 institutions. Patient enrollment began May 16, 1996, and was completed February 17, 1997. The protocol was approved by the institutional review board at all sites. Eligible patients provided written informed consent. Patients were required to have a de novo target coronary artery stenosis of ≥50% in a vessel of diameter 2.75 to 3.5 mm and to be referred for intracoronary stent implantation with an (expected single) 15-mm Palmaz-Schatz stent. Patients were excluded if they had a myocardial infarction within 72 hours before randomization, evident intracoronary thrombus, previous coronary intervention on a nontarget lesion within the past 6 months, planned debulking before stent placement, expected inability to access the

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**TABLE 1. Demographics**

| | Intention to Treat | | | Primary Analysis | | |
|---|---|---|---|---|---|---|
| | Placebo | Abciximab 12-Hour Infusion | Abciximab 24-Hour Infusion | Placebo | Abciximab 12-Hour Infusion | Abciximab 24-Hour Infusion |
| No. of patients | 71 | 79 | 75 | 60 | 66 | 66 |
| Age, y, median (IQR) | 58 (50,67) | 62 (54,72) | 58 (50,68) | 58 (50,67) | 61 (54,71) | 58 (50,67) |
| Female, % | 22.5 | 25.3 | 16.0 | 21.7 | 22.7 | 15.2 |
| Diabetes, % | 11.3 | 12.7 | 18.7 | 8.3 | 13.6 | 16.7 |
| Hypertension, % | 50.7 | 46.8 | 52.0 | 46.7 | 45.5 | 50.0 |
| Smoker (current or quit within 1 y), % | 28.2 | 29.1 | 36.0 | 28.3 | 30.3 | 39.4 |
| Prior PCI, % | 16.9 | 12.7 | 12.0 | 16.7 | 13.6 | 12.1 |
| CCS Angina Class, % | | | | | | |
| I-II | 33.8 | 22.8 | 30.7 | 33.4 | 25.8 | 25.7 |
| III-IV | 52.2 | 55.7 | 62.7 | 53.3 | 57.5 | 66.7 |
| Time to follow-up, d, median (IQR) | 197 (184,211) | 193 (184,213) | 191 (185,214) | 194 (184,209) | 193 (185,213) | 190 (185,212) |

IQR indicates interquartile range; PCI, percutaneous coronary intervention; and CCS, Canadian Cardiovascular Society.
All $P>0.10$.

target lesion by IVUS (eg, calcified plaque, tortuous vessel), or standard contraindications to the use of abciximab.[13]

## Randomization and Drug Regimen

Patients were randomized after the target lesion had been identified by angiography and before first device activation into 1 of 3 groups by sealed envelopes provided by the coordinating center. The physicians involved with the procedure remained blinded to study drug. The treatment regimens were (1) placebo bolus+2 consecutive 12-hour placebo infusions; (2) abciximab 0.25 mg/kg bolus+0.125 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (up to 10 $\mu$g/min maximum) continuous infusion for 12 hours followed by 12-hour placebo infusion; or (3) abciximab 0.25 mg/kg bolus+2 consecutive 12-hour 0.125 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (up to 10 $\mu$g/min maximum) infusions. Patients received ≥200 mg oral aspirin ≥2 hours before the procedure and intravenous heparin titrated to an activated clotting time of 250 to 300 seconds. Aspirin was to be continued for ≥6 months. It was strongly recommended that heparin be discontinued immediately on the completion of the procedure to allow removal of arterial sheaths 4 to 6 hours later. When heparin was continued for clinical indications, it was to be titrated to an activated partial thromboplastin time between 50 and 70 seconds. Ticlopidine use was left to the investigator's discretion. Patients received nitroglycerin 100 to 300 $\mu$g IC immediately before preintervention, postintervention, and follow-up angiograms and IVUS interrogations.

**TABLE 2. Baseline Angiographic Data: Primary Analysis Population**

| | Placebo | Abciximab 12-Hour Infusion | Abciximab 24-Hour Infusion |
|---|---|---|---|
| Lesion location, % | | | |
| LAD | 50.0 | 51.5 | 48.5 |
| LCx | 21.7 | 16.7 | 19.7 |
| RCA | 28.3 | 31.8 | 31.8 |
| Lesion length, mm, median (IQR) | 9 (7,13) | 10 (7,12) | 11 (7,14) |
| Calcification, moderate-severe, % | 13.4 | 12.2 | 12.1 |
| Total occlusion, % | 6.7 | 4.5 | 3.0 |
| Thrombus present, % | 1.7 | 1.5 | 3.0 |
| Modified ACC lesion classification $B_2$ or C, % | 40.0 | 36.4 | 48.4 |

LAD indicates left anterior descending; LCx, left circumflex; RCA, right coronary artery; IQR, interquartile range; and ACC, American College of Cardiology.
All $P>0.10$.

## Stent Implantation Procedure

Stent implantation was performed according to routine clinical practice, aiming for an "optimal" result. To standardize the measurements, a single 15-mm Palmaz-Schatz stent was planned in all cases. If clinically indicated, a second stent could be placed in series with the first. Postdilatation to ≥14 atm was strongly recommended. IVUS guidance was used to confirm optimal placement or suggest further dilatations. The MUSIC criteria (complete stent apposition, symmetrical expansion, and adequate in-stent cross-sectional dimension[16]) were used to define adequate stent expansion.

## Follow-Up Evaluation

Patients were discharged from hospital after completion of study drug infusion and being deemed clinically stable. In-hospital testing included electrocardiography before treatment, at the completion of the stent procedure, and at hospital discharge; platelet count before study drug infusion, at 2, 12, and 24 hours after initiation of study drug, and at hospital discharge; and creatine kinase with MB isoenzymes ≤2 hours before study drug administration and at 8, 16, and 24 hours.

Patients were asked to return for follow-up at 6 months for an assessment of clinical status, electrocardiography, angiography, and IVUS. If the patient required revascularization of the target lesion earlier, angiography and IVUS were to be performed at that time. These results were used as the 6-month results. If stent occlusion occurred within the first 30 days, the patient was excluded from evaluation for the primary efficacy end point. Coronary angiography performed earlier than 4 months was not used for end-point determination unless restenosis or TLR was documented.

## Quantitative IVUS and Angiography

Three IVUS systems were used: Cardiovascular Imaging Systems, Hewlett-Packard and Boston Scientific Corp, and Endosonics. The same instrument type was used for poststent and follow-up imaging.

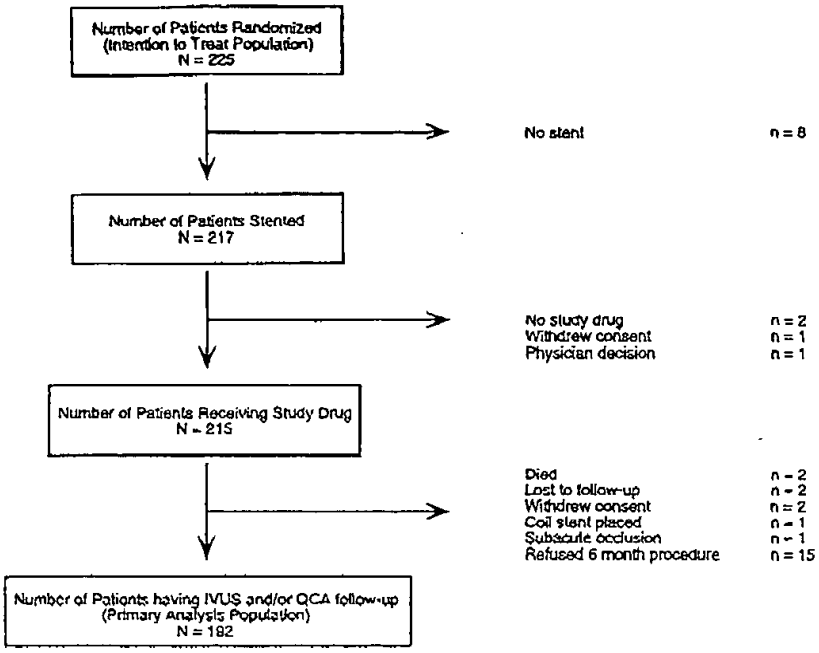


Figure 1. Patient flow in the ERASER study.

Results from the 3 instruments would be expected to be similar.[17] The IVUS examination was performed with motorized pullback of the ultrasound catheter at 0.5 mm/s beginning ≥1 cm distal and continuing to ≥1 cm proximal to the stent(s) with videotape recording.

Ultrasound analysis was performed by the Cardialysis IVUS Core Laboratory by investigators blinded to clinical treatment. A maximum of 200 IVUS images were digitized at a user-defined digitization frame rate (maximum 20 images/s). A minimum-cost algorithm was applied for the automated contour detection of the intimal leading edge and the intracoronary stent boundary. Segments of 3 to 5 mm immediately proximal and distal to the stent were taken as reference diameter. In these segments, the intimal leading edge and external boundary contours (plaque-media) were determined by the algorithm.

Quantitative ultrasound measurements included diameter (mm) and area ($mm^2$) in both the stent and the reference segments. Volumes of the stent, lumen, and intimal hyperplasia are calculated as

$$V=\sum_{i=1}^{N} A_i \times H,$$

where V is volume, A is area of lumen or stent in a given cross-sectional ultrasound image, H is slice thickness, and N is number of digitized cross-sectional images encompassing the volume to be measured. In-stent volume obstruction percent is determined as intimal hyperplasia volume divided by total in-stent volume times 100.[18–20] Intraobserver and interobserver differences in volumetric measurement (nonstented segments) have been reported (n=30; $r$=0.99).[21]

## Angiographic Measurements

Off-line quantitative coronary angiographic (QCA) analysis was performed at the Washington (DC) Hospital Center Angiographic Core Laboratory by investigators blinded to clinical treatment.

**TABLE 3. Treatment**

| | Intention to Treat | | | Primary Analysis | | |
|---|---|---|---|---|---|---|
| | Placebo | Abciximab 12-Hour Infusion | Abciximab 24-Hour Infusion | Placebo | Abciximab 12-Hour Infusion | Abciximab 24-Hour Infusion |
| Maximum ACT, s (IQR) | 328 (284,376) | 335 (302,415) | 338 (307,385) | 324 (285,375) | 330 (302,419) | 340 (309,385) |
| Completed >12 hours of study drug infusion, % | 96.0 | 96.9 | 96.6 | 95.0 | 96.9 | 96.9 |
| Completed full infusion of study drug infusion, % | 94.6 | 90.3 | 92.5 | 95.0 | 93.9 | 92.4 |
| Number of stents placed at target lesion, % | | | | | | |
| 0 | 1.4 | 6.3 | 2.7 | 0.0 | 0.0 | 0.0 |
| 1 | 83.1 | 78.5 | 73.3 | 85.0 | 83.3 | 74.2 |
| 2 | 12.7 | 12.7 | 20.0 | 13.3 | 13.6 | 21.2 |
| >2 | 2.8 | 2.5 | 4.0 | 1.7 | 3.0 | 4.5 |
| Angiographic complications, % | 16.9 | 13.9 | 20.0 | 15.0 | 13.6 | 19.7 |

ACT indicates activated clotting time; IQR, interquartile range. Procedural complications include new thrombus, distal embolization, major dissection, minor dissection, transient occlusion, reduction in TIMI flow from 3 to 2, local perforation, tamponade, side-branch occlusion, other vessel inclusion, spasm, and unsatisfactory stent deployment.

All $P$>0.10.

**TABLE 4. Clinical Outcome**

| | Intention to Treat | | | Primary Analysis | | |
|---|---|---|---|---|---|---|
| | Placebo | Abciximab 12-Hour Infusion | Abciximab 24-Hour Infusion | Placebo | Abciximab 12-Hour Infusion | Abciximab 24-Hour Infusion |
| Event rate through hospital discharge | | | | | | |
| Composite of death, MI, or TLR, % | 11.3 | 5.1 | 9.3 | 10.0 | 6.1 | 9.1 |
| Death | 0 | 0 | 0 | 0 | 0 | 0 |
| MI | 11.3 | 5.1 | 9.3 | 10.0 | 6.1 | 9.1 |
| TLR* | 1.4 | 0 | 0 | 0 | 0 | 0 |
| TIMI major bleed, % | 1.4 | 3.8 | 1.3 | 1.7 | 1.5 | 1.5 |
| Event rate through 6 months | | | | | | |
| Composite of death, MI, or TLR, % | 25.4 | 20.3 | 22.7 | 25.0 | 24.2 | 24.2 |
| Death | 2.8 | 0 | 0 | 0 | 0 | 0 |
| Any MI | 12.7 | 7.6 | 9.3 | 11.7 | 9.1 | 9.1 |
| Q wave MI | 2.8 | 3.8 | 1.3 | 3.3 | 4.5 | 1.5 |
| TLR* | 15.5 | 13.9 | 13.3 | 16.7 | 16.7 | 15.2 |

MI indicates myocardial infarction; TIMI, Thrombolysis in Myocardial Infarction.

*All patients had a repeat percutaneous coronary intervention as the reason for TLR; no patient had coronary artery bypass surgery.

All $P>0.10$.

Cineangiograms were acquired at the clinical sites in multiple, matched projections before and after stent placement and at 6-month follow-up. Standard morphological criteria were used to characterize baseline lesion complexity[22] and angiographic complications.[23]

Cine frames were selected from the 2 "sharpest and most severe" projections of the stenosis before and after stent placement and at late follow-up; sequential cine frames were matched for their position within the cardiac cycle. QCA used the CMS-GFT algorithm.[24] Binary restenosis was defined as a >50% diameter stenosis at follow-up.

## Definitions and End Points

The primary efficacy criterion for the trial was defined as percent in-stent volume obstruction of the target lesion, measured at 6 months by IVUS. Primary safety objectives were defined as major bleeding[25] not associated with bypass surgery through discharge or 7 days, whichever occurred first, and mortality and intracranial hemorrhage through 6 months. Secondary efficacy objectives were defined as target lesion mean and minimum lumen diameter (MLD), late loss and loss index by QCA at 6 months, and a composite of death, myocardial infarction, and TLR within 6 months. Myocardial infarction was defined as (1) new significant Q wave of ≥0.04 seconds or having a depth of ≥25% of the corresponding R wave amplitude in ≥2 contiguous leads or (2) creatine kinase MB ≥3 times the upper limit of normal.

## Study Hypothesis and Statistical Analysis

The primary study hypothesis was that either abciximab dosing regimen would diminish in-stent percent volume obstruction compared with placebo. Previous observation suggested an expected in-stent volume obstruction of 38±24% (Gary Mintz, MD, personal communication). To obtain 80% power to detect an absolute 11% difference between treatment groups, 60 patients per group were required. Assuming that 80% of randomized patients would return for an interpretable 6-month IVUS, the total sample size was 225 patients. The study was not powered to show differences in clinical end points. Patients randomized but not treated with ≥1 stents or study drug or who did not return for angiographic or ultrasound follow-up were excluded from the primary efficacy analysis. Intergroup differences were assessed by ANOVA or $\chi^2$ techniques. Grouping of the 2 abciximab groups for analysis of clinical end points was prespecified. A nominal value of $P<0.05$ was considered

**TABLE 5. IVUS: Primary Analysis Population**

| | Placebo | Abciximab 12-Hour Infusion | Abciximab 24-Hour Infusion |
|---|---|---|---|
| Mean stent CSA, mm² | | | |
| Postprocedure | 8.46±2.09 (51) | 8.92±2.34 (59) | 8.70±2.41 (59) |
| 6-month follow-up | 8.49±2.20 (52) | 9.13±2.12 (54) | 9.10±2.48 (53) |
| Mean lumen CSA at 6-month follow-up, mm² | 6.41±2.27 (52) | 6.82±2.53 (54) | 6.56±2.46 (53) |
| Volume obstruction at 6-month follow-up, %* | 25.10±14.76 (52) | 27.04±15.41 (50) | 29.15±14.16 (52) |
| Minimal lumen CSA, mm² | | | |
| Postprocedure | 6.84±1.89 (51) | 7.14±2.01 (59) | 7.07±1.98 (59) |
| 6-month follow-up | 4.82±2.06 (52) | 4.96±2.40 (54) | 4.64±2.06 (53) |

CSA indicates cross sectional area.

*In 5 patients who had CSA determined, there were technical difficulties in determining stent length for measurement of % volume obstruction.

All values are mean±SD (n); all $P>0.10$.

TABLE 6. QCA: Primary Analysis Population

| | Placebo | Abciximab 12-Hour Infusion | Abciximab 24-Hour Infusion |
|---|---|---|---|
| Reference diameter, mm | | | |
| Preprocedure | 2.94±0.52 | 2.97±0.45 | 3.03±0.52 |
| Postprocedure | 3.00±0.51 | 3.06±0.45 | 3.11±0.52 |
| 6 months | 3.00±0.49 | 2.94±0.52 | 3.09±0.51 |
| MLD, mm | | | |
| Preprocedure | 0.93±0.44 | 0.95±0.43 | 1.03±0.51 |
| Postprocedure | 2.72±0.41 | 2.82±0.42 | 2.87±0.45 |
| 6 months | 2.09±0.64 | 1.96±0.91 | 2.03±0.68 |
| Target lesion stenosis, % | | | |
| Preprocedure | 68±14 | 68±13 | 66±16 |
| Postprocedure | 8±11 | 7±11 | 6±13 |
| 6 months | 30±19 | 34±27 | 34±20 |
| In-stent mean luminal diameter at 6 mo, mm | 2.72±0.56 | 2.55±0.93 | 2.69±0.67 |
| Acute gain, mm | 1.80±0.44 | 1.87±0.53 | 1.84±0.54 |
| Late loss, mm | 0.63±0.58 | 0.88±0.76 | 0.80±0.58 |
| Loss index (late loss/acute gain) | 0.33±0.45 | 0.52±0.51 | 0.47±0.55 |
| In-stent restenosis (≥50%) at 6 months, % | 11.6 | 18.9 | 19.4 |

Values are mean±SD.
All $P>0.10$.

significant. Subset analyses were prespecified only for 3 subgroups: optimal versus suboptimal stent deployment, study drug administration according to protocol or not, and 1 stent at the target lesions versus ≥2 stents.

## Results

### Baseline Characteristics

Baseline patient and angiographic characteristics are shown in Tables 1 and 2. Patient flow through the study is depicted in Figure 1. There were no intragroup differences in any of the measured characteristics.

### Initial Treatment and Outcome

Initial treatments are described in Table 3. Two hundred twenty-two patients (98.7%) received study drug, and 199 (88.4%) completed the study infusion. The median activated clotting time before treatment was 312 seconds. Two hundred seventeen patients (96.4%) received coronary stents. Less than optimal stent deployment by the MUSIC criteria was observed in 45%, 62%, and 67% of the placebo and short and long abciximab groups, respectively ($P$=NS). Angiographic complications were rare and were equally distributed among the treatment groups.

### Clinical Outcomes

Clinical outcomes are described in Table 4. The composite in-hospital end point of death, myocardial infarction, or TLR was seen in 11.3%, 5.1%, and 9.3% in the placebo, short abciximab infusion, and long abciximab infusion groups, respectively. The composite end point of death, myocardial infarction, or TLR at 6 months did not differ among the groups (25.4% placebo versus 21.4% combined abciximab, $P$=NS). TLR predominated in the composite primary clinical end point and occurred in 15.5% of placebo-treated patients and 13.6% of the combined abciximab-treated group ($P$=NS).

### IVUS and QCA

Data for IVUS and QCA are presented in Tables 5 and 6 and are illustrated in Figures 2 and 3. At the completion of the stenting procedure, the treatment groups were well balanced for angiographic percent stenosis. At follow-up, there was no difference in angiographic outcome, with MLDs of 2.7±0.6, 2.6±0.9, and 2.7±0.7 mm in the placebo, 12-hour, and 24-hour abciximab groups, respectively. When measured by IVUS, with or without imputation for target sites that were occluded or tightly stenosed and could not be crossed by the device (placebo, n=5; 12-hour abciximab infusion, n=5; 24-hour abciximab infusion, n=4), there was no difference in the in-stent percent volume obstruction among the 3 groups (see Figure 3). Follow-up IVUS and QCA measurements of mean luminal diameter ($r$=0.83) and MLD ($r$=0.72) were closely correlated. Because of heightened interest engendered by the EPISTENT trial results in diabetics, we also present a post hoc analysis of the primary end-point data, divided into subsets by diabetic status. In-stent volume obstruction for diabetics randomized to placebo was 35±22% (n=3), randomized to 12-hour infusion of abciximab was 27±18% (n=10), and randomized to 24-hour infusion of abciximab was 31±16 (n=13).

## Discussion

This study shows that abciximab, given either at the same dose or for the same dose at a longer duration than that which

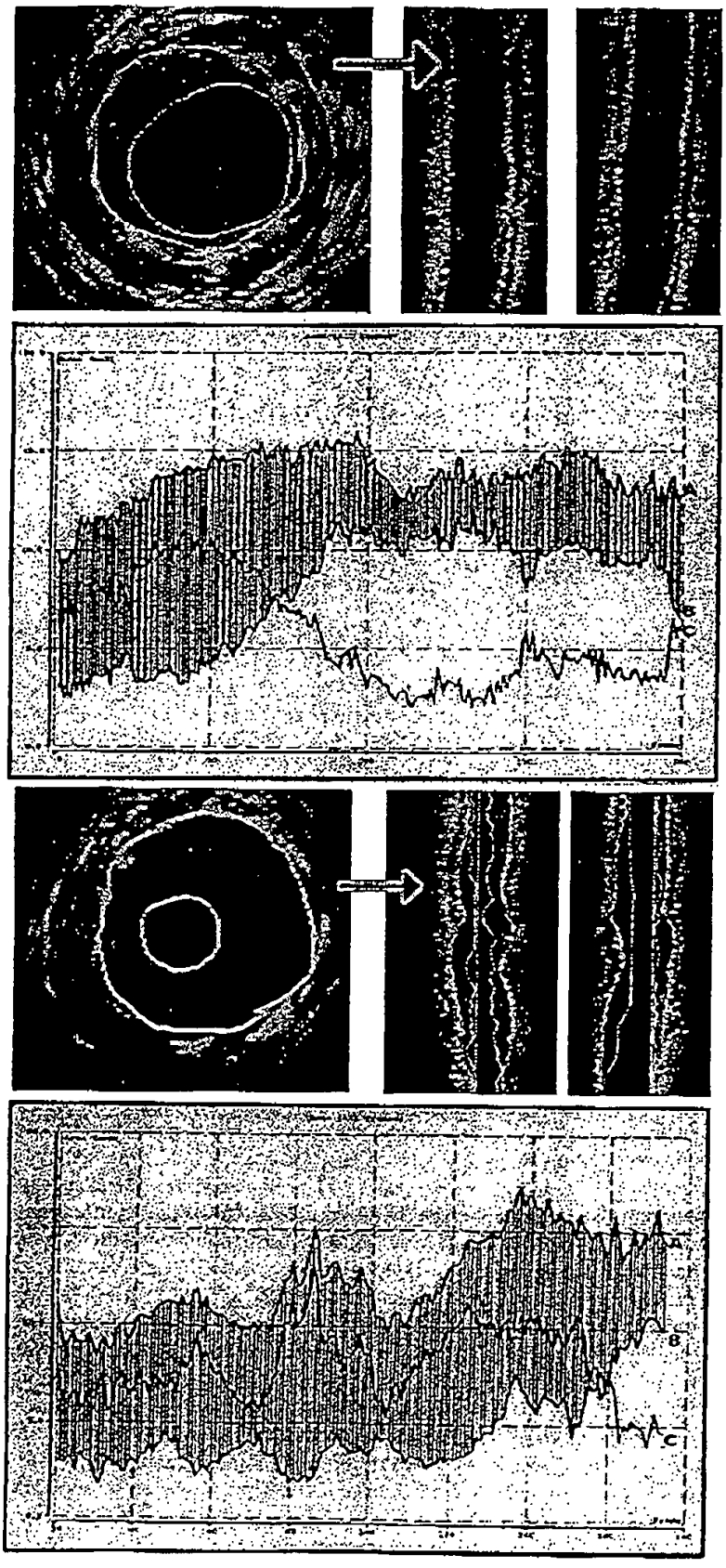

Figure 2. Typical longitudinal IVUS in-stent analysis.

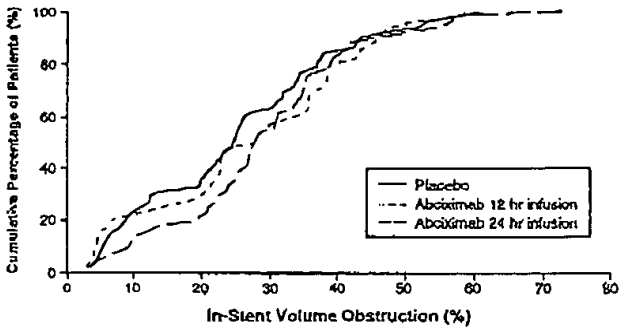


*Figure 3.* Cumulative distribution of the percent in-stent volume obstruction.

decreased TLR at 6 months from 22.3% to 16.5% ($P$=0.007) after balloon angioplasty in the EPIC study,[13] does not reduce neointimal volume after stenting.

This observation enhances our understanding of restenosis after stenting by essentially eliminating 1 putative mechanism, organization of platelet-rich thrombus, and improving our understanding of the role of the $\alpha_v\beta_3$ receptor in that process. At the onset of this study, the abciximab dose used was believed to be likely to inhibit the $\alpha_v\beta_3$ receptor, whose $KD_{50}$ (11±3 nmol) is similar to the platelet $\alpha_{IIb}\beta_3$ receptor.[26] Reconciliation of these data suggests that the dose used was too low or asynchronously timed with a maximal $\alpha_v\beta_3$ receptor expression, or that redundant pathways exist to, in a teleological sense, "protect" the wound-healing process. In fact, recent data suggest that $\alpha_v\beta_3$ receptor expression after arterial injury peaks at 7 to 14 days,[27] after high-level receptor inhibition by abciximab, as used in this study, it diminished.[26,28] Unless the late clinical benefit noted in EPIC was due to happenstance alone, one would have to invoke a different set of mechanisms than those tested in the present study.

This was the first clinical trial to use percent volume coronary obstruction assessed by IVUS as a primary study end point. Our results provide insight into the advantages and disadvantages of this end point instead of percent stenosis or MLD as judged by QCA, or instead of clinical events. IVUS-determined 3D neointimal volume was chosen because it most closely reflects the tissue mass of restenosis, it could be easily measured because of the visibility of the stent to IVUS, and its mean/SD ratio would allow a lower sample size with adequate power to detect a plausible biological difference.

Correlations between IVUS and QCA measurements were good. We did not anticipate the relatively large proportion of patients without follow-up IVUS because of the presence of a high-grade coronary stenosis that made passage of the ultrasound device unsafe or impossible (6.5%) or the relatively large proportion of patients with technically inadequate studies (5.6%). Were a therapeutic intervention to decrease restenosis, the imbalance in the number of lesions that could not be restudied because of failure to pass the ultrasound device would necessitate an acceptable method of imputation for this end point to be useful. Miniaturization of the IVUS probe and further clinical experience should diminish these problems in the future. One must question whether a measurement of the volume of neointima itself or one that on the basis of prior QCA studies (percent area stenosis or minimum cross-sectional area)[29,30] may better correlate with adverse clinical events is better suited as a primary end point for such a trial. Notably, the coefficient of variation (SD/mean) for the QCA data was less than for the IVUS data, implying that on a purely statistical basis, QCA has greater power to detect differences in a given patient population than does IVUS. Finally, a sizable proportion of implanted stents did not meet criteria for "optimal" deployment by the MUSIC criteria. These criteria were infrequently achieved in that study also.[16]

Three other factors may influence the interpretation of this study. First, the results should not necessarily be extrapolated to balloon angioplasty because the mechanisms of restenosis differ.[31,32] Second, we cannot exclude a benefit of larger, and possibly longer, infusion doses of abciximab or of a more powerful or longer-lasting $\alpha_v\beta_3$ receptor inhibitor.[33] Finally, the important reduction in periprocedural myocardial infarction with abciximab noted in the EPIC,[13] EPILOG,[34] and EPISTENT studies,[35] with which our data are consistent, must be considered.

## Appendix

### Steering Committee

Stephen G. Ellis, MD; Mark B. Effron, MD; Herman K. Gold, MD; Martin B. Leon, MD; Jeffrey J. Popma, MD; and Patrick W.J.C. Serruys, MD.

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